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Shahan Islam

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

2550/KIP

Applicant:	Norio MIURA, Noboru YAMAZOE, Taizo UDA	
Serial	No.:08/985,007	Examiner: Christopher L. Chin
Filed:	December 4, 1997	Group Art Unit: 1641
For:	Apparatus for Measuring a Medical Substance; a Sensor for Use in the Apparatus and a Sensing Element for Use in the Sensor	

BRIEF ON APPEAL

ROSENMAN & COLIN LLP
575 MADISON AVENUE
NEW YORK NY 10022-2585
TEL: (212) 940-8564
EMAIL: sislam@rosenman.com

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I. REAL PARTIES IN INTEREST

The real parties in interest are DKK Corporation, Norio MIURA, Noboru YAMAZOE and Taizo UDA.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals and interferences.

III. STATUS OF CLAIMS

Claims 14 to 27 remain.

The application was filed on December 4, 1997 with claims 1 to 13.

Claims 1 to 12 were rejected in an Office Action dated January 22, 1999 and claim 13 was withdrawn from consideration.

Claims 1 to 12 were cancelled and claims 14 to 27 were added in an Amendment dated May 24, 1999.

Claims 14 to 27 were rejected in Final Action dated August 17, 1999.

Claims 14 and 19-24 were amended in an Amendment after Final Action filed on December 10, 1999.

However, the proposed amendment was deemed to raise new issues according to an Advisory Action dated December 27, 1999.

Accordingly, the status of the claims is as they were after the filing of the May 24, 1999 amendment.

IV. STATUS OF AMENDMENTS

Original claims 1 to 12 were rejected in an Office Action dated January 22, 1999 and claim 13 was withdrawn from consideration.

In an Amendment dated May 24, 1999, claims 1 to 12 were cancelled and claims 14 to 27 were added.

Claims 14 to 27 were rejected in "Final Action" dated August 17, 1999.

In an Amendment dated December 10, 1999 after the Final Rejection, claims 14 and 19-24 were amended. However, entry of the amendment was denied as raising new issues as stated in the Advisory Action dated December 27, 1999.

Accordingly, the status of the claims is as they were after the filing of the May 24, 1999 amendment.

V. SUMMARY OF THE INVENTION

The present invention relates to a medical substance measuring apparatus in which a medical substance is measured by using a resonance phenomenon resonating with an evanescent wave and related to a medical substance sensor for use in the apparatus. A major feature of the present invention is that the medical substance to be measured by the apparatus is fixed to a resonance material as an antigen.

In order to measure the medical substance (an antigen) contained in a sample using a resonance phenomenon resonating with an evanescent wave, the apparatus comprises:

a resonance phenomenon generating section having a resonance material; and

a detecting means for detecting a change of an incident light which is made incident upon said resonance material to generate said resonance phenomenon or a change of a reflected light thereof; and

wherein the medical substance (antigen) to be measured is fixed to said resonance material.

This subject matter is defined in claim 14 of the May 24 Amendment, and is described in the specification from page 6, line 7 to page 11, line 11, page 13, line 13 et seq., Embodiment 1 (page 22, line 16 et seq.) and Embodiment 2 (page 32, line 13 et seq.).

Further, the present invention is also directed to a method for measuring the medical substance (an antigen) contained in a sample using a resonance phenomenon resonating with an evanescent wave. The method comprises the steps of:

fixing a medical substance (an antigen) to be measured to a resonance material wherein the resonance phenomenon is caused to resonate with an evanescent wave;

mixing an antibody with said sample wherein the antibody is coupled with said medical substance (antigen) in a specific manner;

bringing a mixture of said antibody and said sample in contact with the resonance material to which said medical substance (antigen) has been fixed;

making a light incident upon said resonance material;

detecting a change of the incident light or a change of a reflected light thereof when said resonance phenomenon is generated; and

recognizing an amount of said medical substance (antigen) contained in said sample on the basis of said change of the incident light or the reflected light.

This subject matter is defined in claim 24 of May 24 Amendment , and is described in the specification from page 6, line 7 to page 11, line 11, and page 13, line 13 et seq., Embodiment 1 (page 22, line 16 et seq.) and Embodiment 2 (page 32, line 13 et seq.).

VI STATEMENT OF ISSUES ON APPEAL

(1) Whether claims 14 to 27 are patentable under 35 U. S. C. § 112, second paragraph.

(2) Whether claims 14, 15, 17, 19, 22, 24, 25 and 27 are patentable under 35 U. S. C. § 102 over Batchelder (U.S. Patent No. 4,844,613), Finlan (U.S. Patent Nos. 4,997,278 and 5,047,213), and Stewart (U.S. Patent No. 5,229,833).

(3) Whether the drawings are allowable as they show every feature of the claimed invention under 37 CFR 1.83 (a).

VI. GROUPING OF CLAIMS

Although independent claims 14, 22 and 24 show the main features of the invention, dependent claims 15 to 21, 23, and 25 to 27 are believed to be separately patentable.

VII. ARGUMENT

This is a brief supporting an appeal from Final Rejection dated August 17, 1999, in which:

(a) claims 14 to 27 were rejected under 35 U.S.C. § 112, second paragraph;

(b) claims 14, 15, 17, 19, 22, 24, 25 and 27 were rejected under 35 U.S.C. § 102 over Batchelder, Finlan and Stewart; and

(c) the drawings were objected to because they do not show every feature of the claimed invention under 37 CFR 1.83 (a).

In the Advisory Action, the Examiner deemed that the amendment dated December 10, 1999 after Final Action raised new issues and therefore did not enter them. Accordingly, the status of the claims is as they were upon the submission of the first amendment dated May 24, 1999.

Applicant respectfully submits, however, that the new issue ruling was in error.

This brief is accordingly divided as follows:

(a) Part I demonstrates that the rejection in view of the May 24 Amendment was in error and that claims 14- 27 therein violate neither Sections 112 nor 102; and

(b) alternatively, Part II demonstrates that:

(i) claims 14-27 as presented in the Amendment After Final satisfy the requirements of Sections 112 and 102; and

(ii) the new issue determination in the Advisory Action was erroneous.

PART I - THE REJECTION IN VIEW OF THE MAY 24 AMENDMENT WAS IN ERROR AS CLAIMS 14- 27 THEREIN VIOLATE NEITHER SECTIONS 112 NOR 102

A. THE §112 REJECTION SHOULD BE WITHDRAWN

Claims 14-27 were rejected as being unpatentable under 35 U. S. C. § 112, second paragraph. Such rejection should be withdrawn for the following reasons.

First, the Examiner pointed out that it was not clear from the last line of claim 14 whether the antigen fixed to the resonance material is "a medical substance," or a reagent for detection of the medical substance. The last line of claim 14 in the May 24 Amendment reads as follows:

"wherein **the medical substance** to be measured is fixed to said resonance material **as an antigen**."

Therefore, claim 14 clearly defines that the antigen fixed to the resonance material is "a medical substance," not a reagent for detection of the medical substance.

Further, the Examiner asserts that, "if the antigen is the 'medical substance', then a corresponding antibody specific for the antigen would have to be present on the resonance material to permit detection of the antigen." It is respectfully submitted that the Examiner's assertion is proper for the conventional detecting technology. However, as described above, the present invention has, as a feature, that not the antibody but the antigen i.e., medical substance is fixed to the resonance material. This is vastly different from conventional technology, because such construction makes it easy to detect the medical substance having a very low molecular weight. The antibody specific for the antigen is therefore not required on the resonance material.

The Examiner rejected claim 22 as it suffers from the same deficiency as claim 14. Applicant respectfully submits however that the rejection of claim 22 should be withdrawn for the same reasons as mentioned above for claim 14.

Next, the Examiner rejected claims 19-21 because claim 19 depends on canceled claim 2. Applicant has corrected the errors in the December 10 Amendment to depend claim 19 properly on claim 14.

Furthermore, the Examiner asserts that, in claims 20 and 23, it is not clear as to how the antigen can be fixed to a surface of the metal film which is opposite to the surface prism when the metal film is formed on the surface of the prism, and therefore that the claims fail to recite the presence of another metal film that is positioned opposite the metal film on the surface of the prism to support the antigen. However, with respect to the structures of the medical substance, metal film and prism, claims 20 and 23 recite that "**the medical substance** to be measured is **fixed** as an antigen **to another surface of said metal film which is opposite to the surface on which said prism is formed**."

Accordingly, such an Examiner's understanding is incorrect, because there is no metal film that is positioned opposite the metal film on the surface of the prism to support the antigen and it is therefore not necessary to recite the presence of another metal film.

Therefore, though the Examiner objected to the drawings for the reason that the antigen fixed to another metal film in claims 20 and 23 must be shown, the objection to the drawings should be withdrawn, for the reasons stated above.

Further, the Examiner asserts that claim 24 is vague as to whether the antigen is "a medical substance," or a reagent for detection of the medical substance. Lines 4-5 of claim 24 in the May 24 Amendment read as follows:

"fixing **a medical substance** to be measured to a resonance material wherein a resonance phenomenon is caused to resonate with an evanescent wave **as an antigen.**"

Therefore, claim 24 clearly defines that the antigen is "a medical substance," not a reagent for detection of the medical substance, as explained above for claim 14.

Also, the Examiner asserts that lines 6-7 of claim 24 are not clear as to whether the antibody is coupled with the medical substance or the sample, and is specific for the antigen or the medical substance. Lines 6-7 of claim 24 in the May 24th Amendment read as follows:

"mixing **an antibody which is coupled with said fixed medical substance in a specific manner** to said sample."

Therefore, claim 24 clearly defines that the antibody is coupled with the medical substance and is specific for the medical substance which is the antigen.

With respect to the mixture recited in lines 8-9 of claim 24, the Examiner deems it to lack antecedent support and to be redundant because the sample and antibody are already in contact with the resonance material. Lines 8-9 of claim 24 in the May 24 Amendment read as follows:

"bringing the mixture in contact with the resonance material to which said medical substance has been fixed."

The mixture recited in lines 8-9 of claim 24 means the mixture of said antibody and said sample defined in lines 6-7. Further, when mixing the antibody and the sample, some of the antibody is coupled with said medical substance contained in the sample in a specific manner, and when the mixture is brought in contact with the resonance material to which the medical substance has been fixed, the rest of the antibody is coupled with the fixed medical substance in a specific manner. Therefore, the step recited in lines 8-9 of claim 24 is not redundant but an essential step of the claimed invention.

Further, the Examiner asserts that lines 11-12 of claim 24 are vague because any change in the properties of the incident light is the result of "medical substance" and antibodies being bound to the resonance material which is not clearly set forth in the detection step recited in these two lines. However, lines 11-12 of claim 24 read as follows:

> **"detecting a change of the incident light or a change of a reflected light thereof when said resonance phenomenon is generated;"**

Claim 24 therefore clearly defines that a change of the incident light or a change of a reflected light thereof is detected by using the resonance phenomenon generated by the previous steps in lines 1-10 when an antibody-antigen reaction is caused.

In view thereof, all of the above-mentioned claims particularly point out and distinctly claim the subject matter of the invention. Such rejection under §112 should therefore be withdrawn and all of the above-mentioned claims are allowable.

Each remaining claim is dependent directly or indirectly on claims 14, 22 and 24, and is also allowable for the same reasons.

B. THE REJECTION IN VIEW OF THE REFERENCES SHOULD BE WITHDRAWN

The Examiner asserted claims 14, 15, 17, 19, 22, 24, 25 and 27 are unpatentable under 35 U. S. C. § 102 because the claims are anticipated by Batchelder (U.S. Patent No. 4,844,613), Finlan (U.S. Patent Nos. 4,997,278 and 5,047,213), and Stewart (U.S. Patent 5,229,833). As demonstrated herein, the rejection of the May 24 Amendment was in error and the rejected claims do not violate Section 102.

1. BATCHELDER DOES NOT DISCLOSE, TEACH OR OTHERWISE SUGGEST MANY EXPLICITLY RECITED CLAIM FEATURES

Batchelder et al (U.S. Patent No. 4,844,613) is directed to an optical sensor device for detecting the presence of a specific material by using surface plasmon resonance phenomenon.

A transparent body is coated with a thin gold film which film may be coated with an antibody (see abstract).

In contrast to Batchelder et al. in the claimed invention, it is not an antibody but **antigen** fixed to a surface of a metal film. The reference does not disclose, teach or otherwise suggest a measuring apparatus or sensor where an antigen to be measured is fixed to a surface of a metal film or a resonance material as recited in independent claims 14, 22 and 24.

Nonetheless, the Examiner asserts that the current claims do not clearly define the differences between the claimed invention and the reference, *i.e.*, the presence of an antigen on the resonance material, wherein the antigen is the analyte to be detected.

However, the last two lines of claims 14 and 22 in the May 24 Amendment read as follows:

> "wherein **the medical substance to be measured is fixed to said resonance material as an antigen.**"

Therefore, claims 14 and 22 clearly define that the medical substance fixed to the resonance material is "an antigen."

Further, lines 4-5 of claim 24 in the May 24 Amendment read as follows:

> **"fixing a medical substance to be measured to a resonance material** wherein a resonance phenomenon is caused to resonate with an evanescent wave **as an antigen**."

Therefore, claim 24 clearly defines that the medical substance fixed to the resonance material is the antigen. Thus, the claimed invention clearly defines the difference from the reference, *i.e.*, the presence of an antigen on the resonance material.

Further, according to the present invention, such a medical substance having an extremely small molecular weight, which is difficult to detect by the conventional technique, can be easily detected and is thus clearly non-obvious over the prior art.

As mentioned in the specification on page 4, line 28 to page 5, line 24, according to previously known methods, it has been tried to measure a medical substance wherein an antibody is fixed to a resonance material, such as a metal thin film, and the medical substance which is coupled to the antibody in a specific manner is detected directly. However, the medical substance contained in a body liquid, such as urine or blood, has a significantly small molecular weight; therefore, even if the medical substance reacts with the antibody fixed to the resonance material, the change of the resonance angle, etc. is extremely small. Therefore, it is very difficult to detect such a medical substance by conventional methods.

By contrast, the present invention provides an apparatus for detecting a medical substance using a resonance phenomenon resonating with an evanescent wave, by which even a medical substance having a small molecular weight can be detected. In accordance with the present invention, a medical substance to be measured by the apparatus is previously fixed to the resonance material as an antigen; a known amount of an antibody is mixed in a sample; the antibody is brought into contact with the resonance material on which the antigen (medical substance to be detected) has been fixed; then the change of the condition for generating the resonance phenomenon (resonance angle, etc.) is observed when an antigen-antibody reaction is caused. Since an antibody has a significantly greater molecular weight, when such an antibody is coupled with the antigen (medical substance to be detected) fixed on the resonance material, the change of the condition, i.e. resonance angle, etc. is sufficiently great to be detected. It should be noted that the amount of the antibody mixed in the sample is previously known, so that

the amount of the medical substance contained in the sample can be indirectly calculated from the change of the condition. Therefore, according to the invention, a sufficient sensitivity can be obtained in the measurement of a medical substance having an extremely small molecular weight contained in a sample, because the antibody, which is coupled with the antigen (medical substance) fixed to the resonance material, has a sufficient molecular weight to largely change the resonating condition. This is clearly proved in the embodiments mentioned in the original specification.

Therefore, inasmuch as the present invention has a distinctive feature that not an antibody but an antigen is fixed on the resonance material, this is totally different from the conventional technology, because such construction makes it easy to detect the medical substance having a very small molecular weight.

In view thereof, Batchelder clearly teaches away from the invention. See, e.g., In re Hedges, 783 F.2d 1038 (Fed. Cir. 1986) (Teaching away from the invention by the prior art is indicative of non-anticipation and non-obviousness). Monarch Knitting Machinery Corp. v. Fukuhara Industrial & Trading Co. Ltd., 139 F.3d 977 (Fed. Cir. 1998).

Therefore, independent claims 14, 22 and 24, which recite the distinctive features, are not anticipated by Batchelder and thus they are allowable.

Each remaining claim is dependent, directly or indirectly, on claims 14, 22 and 24, and is also allowable for the same reasons.

2. **FINLAN AND STEWART FAIL TO TEACH OR SUGGEST THE INVENTION**

The Examiner further asserted claims 14, 15, 17, 19, 22, 24, 25 and 27 are unpatentable under 35 U. S. C. § 102 because the claims are anticipated by Finlan et al (U.S. Patent Nos. 4,997,278 and 5,047,213), and Stewart (U.S. Patent No. 5,229,833).

However, Finlan et al (U.S. Patent Nos. 4,997,278 and 5,047,213) are directed to sensors using the principle of surface plasmon resonance (SPR) to monitor the progress of the reaction between a sample and a sensitive layer, for example an antibody layer (see abstracts).

Accordingly, Finlan does not disclose, teach or otherwise suggest the distinctive feature of the claimed invention that the antigen is fixed on the resonance material.

Similarly, Stewart also fails to teach the above characteristics of the invention. Stewart is related to an optical sensor. A resonance mirror device used in the optical sensor consists of a prism structure onto which one low and one high index dielectric film is deposited. In accordance with Stewart, antibodies for the species to be detected are immobilized onto the surface of the prism, and the species bind to the antibody layer (see column 4, lines 34-56). Therefore, Stewart fails to disclose or teach the distinctive feature of the claimed invention that the antigen is fixed on the resonance material.

Lack of teaching or suggestion in the art for key claimed features is indication of non-anticipation and non-obviousness (See e.g. ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572 (Fed. Cir. 1984); In re Rouffet, 149 F.3d 1350 (Fed. Cir. 1998).

In view of the above, the prior art, alone or in combination, fails to disclose, teach or even remotely suggest the invention. Accordingly, the rejection in view of the references should be withdrawn and independent claims 14, 22 and 24 are allowable.

Each remaining claim is dependent on claims 14, 22 and 24, directly or indirectly and is also allowable for the same reasons.

PART II - THE NEW ISSUE DETERMINATION WAS IN ERROR AND CLAIMS 14- 27 (AS ALTERNATIVELY PRESENTED) VIOLATE NEITHER SECTIONS 112 NOR 102

A. THE §112 REJECTION SHOULD BE WITHDRAWN

Part I, Section A. addresses, in detail, why the claims clearly define and particularly point out the subject matter of the invention. Such arguments are also applicable here, because the distinctions pointed to in claims 14-27 of the May 24 Amendment are also present in claims 14-27 of the December 10 Amendment as alternatively presented herein. Accordingly, the arguments of Part I, Section A. are incorporated herein by reference as though fully set forth.

As explained, claims 14-27 are being presented here in the alternative, because it is submitted (and demonstrated in Section II. C. infra) that the Amendment presented after the Final Action (with some minor changes to place it in better form for appeal) does not raise "new issues." The amendments are quite minor and merely clarify the invention. The sole substantive amendment of "a medical substance" into "a medical substance (an antigen)" is only to make clear that the medical substance fixed to the resonance material is the antigen and that an antibody is coupled with the antigen in a specific manner, because the Examiner is confused with those features.

Applicant now therefore demonstrates herein how, in addition to the arguments in Part I, Section A, claims 14-27 as alternatively presented in the Amendment after the Final Action, clearly define and particularly point out the subject matter of the invention.

Claims 14-27 were rejected as being unpatentable under 35 U. S. C. § 112, second paragraph. Such rejection should be withdrawn for the following reasons.

First, the Examiner pointed out that that the last line of claim 14 is not clear as to whether the antigen fixed to the resonance material is "a medical substance," or a reagent for detection of the medical substance. The last line of claim 14 in the December 10 Amendment reads as follows:

"wherein **the medical substance (antigen)** to be measured is fixed to said resonance material."

Claim 14 therefore clearly defines that the antigen fixed to the resonance material is "a medical substance," not a reagent for detection of the medical substance.

As the Examiner appears to assert that the current claims do not clearly define the presence of an antigen on the resonance material wherein the antigen is the analyte that is to be detected, applicant has amended claim 14 to clarify the points mentioned by the Examiner.

Further, the Examiner asserts that, "if the antigen is the 'medical substance', then a corresponding antibody specific for the antigen would have to be present on the resonance material to permit detection of the antigen." It is respectfully submitted that the Examiner's assertion is proper for the conventional detecting technology. However, as described above, the present invention has a feature that it is not the antibody but the antigen i.e., medical substance which is fixed to the resonance material. This is vastly different from the conventional technology because such construction makes it easy to detect medical substance having a very small molecular weight. Therefore, the antibody specific for the antigen is not required on the resonance material.

The Examiner rejected claim 22 as it suffers from the same deficiency as claim 14. However, Applicant respectfully submits that the rejection of claim 22 should be withdrawn for the same reasoning as mentioned above for claim 14.

Next, the Examiner rejected claims 19-21 because claim 19 depends on canceled claim 2. Accordingly, Applicant corrected the errors in the December 10 Amendment to properly depend claim 19 on claim 14.

Furthermore, the Examiner asserts that, in claims 20 and 23, it is not clear how the antigen can be fixed to a surface of the metal film which is opposite to the surface prism when the metal film is formed on the surface of the prism and therefore that the claims fail to recite the presence of another metal film that is positioned opposite the metal film on the surface of the prism to support the antigen. However, with respect to the structures of the medical substance, metal film and prism, claims 20 and 23 recite that "**the medical substance (antigen)** to be measured is **fixed to a surface of said metal film**."

Accordingly, it is submitted that the Examiner's understanding is incorrect, because there is no metal film that is positioned opposite the metal film on the surface of the prism to support the antigen and therefore it is not necessary to recite the presence of another metal film.

Therefore, though the Examiner objected to the drawings for the reason that the antigen fixed to another metal film in claims 20 and 23 must be shown, the objection to the drawings should be withdrawn, for the same reasons stated above.

Further, the Examiner asserts that claim 24 is vague as to whether the antigen is "a medical substance," or a reagent for detection of the medical substance. Lines 4-5 of claim 24 in December 10 Amendment read as follows:

> "fixing **a medical substance (antigen)** to be measured to a resonance material wherein the resonance phenomenon is caused to resonate with an evanescent wave."

Therefore, claim 24 clearly defines that the antigen is "a medical substance," not a reagent for detection of the medical substance, as explained above for claim 14.

Also, the Examiner asserts that lines 6-7 of claim 24 are not clear as to whether the antibody is coupled with the medical substance or the sample, and is specific for the antigen or the medical substance. Lines 6-7 of claim 24 in the December 10 Amendment read as follows:

"mixing an antibody with said sample wherein the antibody is coupled with said medical substance (antigen) in a specific manner."

Therefore, claim 24 clearly defines that the antibody is coupled with the medical substance (antigen) and also is specific for the medical substance (antigen).

With respect to the mixture recited in lines 8-9 of claim 24, the Examiner deems it to lack antecedent support and to be redundant because the sample and antibody are already in contact with the resonance material. Lines 8-9 of claim 24 in December 10 Amendment read as follows:

"bringing a mixture of said antibody and said sample in contact with the resonance material to which said medical substance (antigen) has been fixed."

The mixture recited in lines 8-9 of claim 24 means the mixture of said antibody and said sample defined in lines 6-7. Further, when mixing the antibody and the sample, some of the antibody is coupled with said medical substance contained in the sample in a specific manner, and when the mixture is brought in contact with the resonance material to which said medical substance has been fixed, the rest of the antibody is coupled with the fixed medical substance in a specific manner. Therefore, the step recited in lines 8-9 of claim 24 is <u>not</u> redundant but an essential step of the claimed invention.

Further, the Examiner asserts that lines 11-12 of claim 24 are vague because any change in the properties of the incident light is the result of "medical substance" and antibodies being bound to the resonance material which is not clearly set forth in the detection step recited in these two lines. However, lines of 11-12 of claim 24 read as follows:

"detecting a change of the incident light or a change of a reflected light thereof when said resonance phenomenon is generated."

Therefore, claim 24 clearly defines that a change of the incident light or a change of a reflected light thereof is detected by using the resonance phenomenon generated by the previous steps in lines 1-10 when an antibody-antigen reaction is caused.

In view thereof, all of the above-mentioned claims particularly point out and distinctly claim the subject matter of the invention. Therefore, such rejection under §112 should be withdrawn and all of the above-mentioned claims are allowable.

Each remaining claim is dependent directly or indirectly on claims 14, 22 and 24, and is also allowable for the same reasons.

B. THE REJECTION IN VIEW OF THE REFERENCES SHOULD BE WITHDRAWN

The Examiner asserted claims 14, 15, 17, 19, 22, 24, 25 and 27 are unpatentable under 35 U. S. C. § 102 because the claims are anticipated by Batchelder (U.S. Patent No. 4,844,613), Finlan (U.S. Patent Nos. 4,997,278 and 5,047,213), and Stewart (U.S. Patent No. 5,229,833).

In Part I, Section B., applicant fully explained the differences between the claimed invention and the prior art. Such arguments are also applicable here, because the distinctive features pointed to in claims 14-27 of the May 24 Amendment are also present in claims 14-27 of the December 10 Amendment as alternatively presented herein. The Amendment presented after the Final Action does not raise any new issues as it has only some minor changes to place it in better form and to clarify the Examiner's points. The sole substantive amendment of "a medical substance----as an antigen" into "a medical substance (antigen)" is only to make clear that the medical substance fixed to the resonance material is the antigen and that an antibody is coupled with the antigen in a specific manner, because the Examiner is confused with those features.

Accordingly, the arguments of Part I, Section B. are incorporated herein by reference as though fully set forth.

1. **BATCHELDER TEACHES AWAY FROM THE INVENTION**

As explained in the above Part I, Section B., Batchelder et al teaches an optical sensor device for detecting the presence of a specific material by using surface plasmon resonance phenomenon. A transparent body is coated with a thin gold film which film may be coated with an antibody (see abstract).

In contrast to Batchelder et al, in the claimed invention, an antigen is fixed to a surface of a metal film. Thus, the reference does not disclose, teach or otherwise suggest a measuring apparatus or sensor where an antigen (a medical substance) to be measured is fixed to a surface of a metal film or a resonance material as recited in independent claims 14, 22 and 24.

Nonetheless, the Examiner asserts that the current claims do not clearly define the differences between the claimed invention and the reference, *i.e.*, the presence of an antigen on the resonance material, wherein the antigen is the analyte that is to be detected.

Accordingly, in order to make clear that the medical substance is an antigen, applicant amended the last two lines of claims 14 and 22 in the December 10 Amendment as follows:

> "wherein **the medical substance (antigen) to be measured is fixed to said resonance material.**"

Therefore, claims 14 and 22 clearly define that "the medical substance" fixed to the resonance material is "an antigen."

Further, lines 4-5 of claim 24 in the December 10 Amendment read as follows:

> "**fixing a medical substance (an antigen) to be measured to a resonance material** wherein the resonance phenomenon is caused to resonate with an evanescent wave."

Therefore, claim 24 clearly defines that the medical substance fixed to the resonance material is the antigen. Thus, the claimed invention clearly defines the differences from the reference, *i.e.*, the presence of an antigen on the resonance material.

In as much as the present invention has a distinctive feature that not an antibody but an antigen is fixed on the resonance material, this is totally different from the conventional technology, because such construction makes it easy to detect the medical substance having a very small molecular weight.

In view thereof, Batchelder clearly teaches away from the invention. Therefore, independent claims 14, 22 and 24, which recite the distinctive features, are allowable.

Each remaining claim is dependent, directly or indirectly, on claims 14, 22 and 24, and is also allowable for the same reasons.

2. **FINLAN AND STEWART FAIL TO TEACH OR SUGGEST THE INVENTION**

The Examiner further asserted claims 14, 15, 17, 19, 22, 24, 25 and 27 are unpatentable under 35 U. S. C. § 102 because the claims are anticipated by Finlan et al (U.S. Patent Nos. 4,997,278 and 5,047,213), and Stewart (U.S. Patent No. 5,229,833).

However, Finlan et al (U.S. Patent Nos. 4,997,278 and 5,047,213) are directed to sensors using the principle of surface plasmon resonance (SPR) to monitor the progress of the reaction between a sample and a sensitive layer, for example an antibody layer (see abstracts).

Accordingly, Finlan does not disclose, teach or otherwise suggest the distinctive feature of the claimed invention that the antigen is fixed on the resonance material.

Similarly, Stewart also fails to teach the above characteristics of the invention. Stewart is related to an optical sensor. A resonance mirror device used in the optical sensor consists of a prism structure onto which one low and one high index dielectric film is deposited. In accordance with Stewart, antibodies for the species to be detected are immobilized onto the

surface of the prism, and the species bind to the antibody layer (see column 4, lines 34-56). Therefore, Stewart fails to disclose or teach the distinctive feature of the claimed invention that the antigen is fixed on the resonance material.

In view of the above, the prior art, alone or in combination, fails to disclose, teach or even remotely suggest the invention. Accordingly, the rejection in view of the references should be withdrawn and independent claims 14, 22 and 24 are allowable.

Each remaining claim is dependent on claims 14, 22 and 24, directly or indirectly and is also allowable for the same reasons.

C. THE AMENDMENTS AFTER FINAL ACTION DID NOT RAISE NEW ISSUES

In the Advisory Action, the Examiner pointed out that "the amendments to claim 14 (a positive recitation of a medical substance on the resonance material) raises new issues-112 2nd paragraph because the claimed apparatus cannot detect a medical substance in a sample when the claim now recites the medical substance as already being part of the claimed apparatus."

However, the Amendment presented after the Final Action is only to clarify the Examiner's points. The Examiner pointed out that the last line of claim 14 is not clear as to whether the antigen fixed to the resonance material is a medical substance, or a reagent for detection of the medical substance. The last line of claim 14 in the May 24 Amendment reads as follows:

> "wherein **the medical substance to be measured is fixed to said resonance material as an antigen.**"

Therefore, claim 14 clearly defines that the antigen fixed to the resonance material is a medical substance, not a reagent for detection of the medical substance.

Nonetheless, the Examiner maintained the rejection in a Final Action and therefore, applicant amended claim 14 as follows:

"wherein **the medical substance (antigen) to be measured is fixed to said resonance material.**"

Thus, the sole substantive amendment of "a medical substance------as an antigen" into "a medical substance (antigen)" is only to make clear that the medical substance fixed to the resonance material is the antigen, because the Examiner is confused with this feature. Accordingly, the Amendment after the Final Action changing "as an antigen" to "(antigen)" does not raise any new issues and should be deemed to place the application in better form for appeal by simplifying the issues for appeal.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the Examiner's rejection of claims 14 to 27 be reversed.

Respectfully submitted,
ROSENMAN & COLIN LLP

Shahan Islam, Esq. (Reg No. 32,507)

Dated: May 11, 2000
575 MADISON AVENUE
NEW YORK NY 10022-2585
TEL: (212) 940-8564
EMAIL: sislam@rosenman.com

APPENDIX I - CLAIMS

14. (as of May 24 Amendment) An apparatus for measuring a medical substance contained in a sample using a resonance phenomenon resonating with an evanescent wave, said apparatus, comprising:

a resonance phenomenon generating section having a resonance material; and

a detecting means for detecting a change of an incident light which is made incident upon said resonance material to generate said resonance phenomenon or a change of a reflected light thereof; and

wherein the medical substance to be measured is fixed to said resonance material as an antigen.

15. An apparatus according to claim 14, wherein said change to be detected by said detecting means is an incident angle of said light being made incident upon said resonance material when an intensity of the reflected light thereof is decreased.

16. An apparatus according to claim 14, wherein said change to be detected by said detecting means is a wavelength or a wave number of said reflected light when an intensity of said reflected light is decreased.

17. An apparatus according to claim 14, wherein said change to be detected by said detecting means is an intensity of said reflected light when the incident light is made incident upon said resonance material with a predetermined incident angle.

18. An apparatus according to claim 14, wherein said change to be detected by said detecting means is an incident angle of said incident light when a phase of said reflected light is varied.

19. An apparatus according to claim 2, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

20. An apparatus according to claim 19, wherein said resonance phenomenon generating section comprises a prism having a high refractive index, a thin metal film directly or indirectly formed on one of said prism as said resonance material, and a light source for making a light incident upon said metal film via said prism, wherein the medical substance to be measured is fixed as an antigen to another surface of said metal film which is opposite to the surface on which said prism is formed.

21. An apparatus according to claim 20 further comprising a calculating means for recognizing an amount of said medical substance contained in said sample in accordance with the change detected by said detecting means.

22. A medical substance sensor for use in an apparatus for measuring a medical substance contained in a sample using a resonance phenomenon resonating with an evanescent wave comprising a resonance material where a resonance phenomenon is caused to resonate with an evanescent wave, wherein the medical substance to be measured is fixed to said resonance material as an antigen.

23. A medical substance sensor according to claim 22 further comprising a prism having a high refractive index, a thin metal film which is directly or indirectly formed on one of the surfaces of said prism as said resonance material, wherein the medical substance to be measured is fixed as an antigen to another surface of said metal film which is opposite to the surface on which said prism is formed.

24. A method for measuring a medical substance contained in a sample using a resonance phenomenon resonating with an evanescent wave, said method comprising the steps of:

fixing a medical substance to be measured to a resonance material wherein a resonance phenomenon is caused to resonate with an evanescent wave as an antigen;

mixing an antibody which is coupled with said fixed medical substance in a specific manner to said sample;

bringing the mixture in contact with the resonance material to which said medical substance has been fixed;

making a light incident upon said resonance material;

detecting a change of the incident light or a change of a reflected light thereof when said resonance phenomenon is generated; and

recognizing an amount of medical substance contained in said sample on the basis of said change of the incident light or the reflected light.

25. A method for measuring a medical substance according to claim 24, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

26. An apparatus according to claim 16, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

27. An apparatus according to claim 17, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

APPENDIX II – CLAIMS

14. (as of December 10 Amendment) An apparatus for measuring a medical substance (an antigen) contained in a sample using a resonance phenomenon resonating with an evanescent wave, said apparatus, comprising:

a resonance phenomenon generating section having a resonance material; and

a detecting means for detecting a change of an incident light which is made incident upon said resonance material to generate said resonance phenomenon or a change of a reflected light thereof

wherein the medical substance (antigen) to be measured is fixed to said resonance material.

15. An apparatus according to claim 14, wherein said change to be detected by said detecting means is an incident angle of said light being made incident upon said resonance material when an intensity of the reflected light thereof is decreased.

16. An apparatus according to claim 14, wherein said change to be detected by said detecting means is a wavelength or a wave number of said reflected light when an intensity of said reflected light is decreased.

17. An apparatus according to claim 14, wherein said change to be detected by said detecting means is an intensity of said reflected light when the incident light is made incident upon said resonance material with a predetermined incident angle.

18. An apparatus according to claim 14, wherein said change to be detected by said detecting means is an incident angle of said incident light when a phase of said reflected light is varied.

19. An apparatus according to claim 14, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

20. An apparatus according to claim 19, wherein said resonance phenomenon generating section comprises a prism having a high refractive index, a thin metal film directly or indirectly formed on one of the surfaces of said prism as said resonance material, and a light source for making a light incident upon said metal film via said prism, wherein the medical substance (antigen) to be measured is fixed to a surface of said metal film.

21. An apparatus according to claim 20 further comprising a calculating means for recognizing an amount of said medical substance (antigen) contained in said sample in accordance with the change detected by said detecting means.

22. A medical substance sensor for use in an apparatus for measuring a medical substance (an antigen) contained in a sample using a resonance phenomenon resonating with an evanescent wave comprising a resonance material where the resonance phenomenon is caused to resonate with an evanescent wave, wherein the medical substance (antigen) to be measured is fixed to said resonance material.

23. A medical substance sensor according to claim 22 further comprising a prism having a high refractive index, a thin metal film which is directly or indirectly formed on one of the surfaces of said prism as said resonance material, wherein the medical substance (antigen) to be measured is fixed to a surface of said metal film.

24. A method for measuring a medical substance (an antigen) contained in a sample using a resonance phenomenon resonating with an evanescent wave, said method comprising the steps of:

fixing a medical substance (an antigen) to be measured to a resonance material wherein the resonance phenomenon is caused to resonate with an evanescent wave;

mixing an antibody with said sample wherein the antibody is coupled with said medical substance (antigen) in a specific manner;

bringing a mixture of said antibody and said sample in contact with the resonance material to which said medical substance (antigen) has been fixed;

making a light incident upon said resonance material;

detecting a change of the incident light or a change of a reflected light thereof when said resonance phenomenon is generated; and

recognizing an amount of said medical substance (antigen) contained in said sample on the basis of said change of the incident light or the reflected light.

25. A method for measuring a medical substance according to claim 24, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

26. An apparatus according to claim 16, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.

27. An apparatus according to claim 17, wherein said resonance phenomenon is a surface plasmon resonance phenomenon.